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| 60/355,145 | 8 February 2002 (08.02.2002) | US |
| 60/355,257 | 8 February 2002 (08.02.2002) | US |
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- (72) Inventors; and
- (75) Inventors/Applicants (for US only): AFAR, Daniel [CA/US]; 435 Visitacion Avenue, Brisbane, CA 94005 (US). AZIZ, Natasha [US/US]; 411 California Avenue, Palo Alto, CA 94306 (US). GISH, Kurt, C. [US/US]; 37 Artuna Avenue, Piedmont, CA 94611 (US). HEVEZI, Peter, A. [GB/US]; 1360 11th Avenue, San Francisco, CA 94122 (US). MACK, David, H. [US/US]; 2076 Monterey Avenue, Menlo Park, CA 94025 (US). WILSON, Keith, E. [US/US]; 219 Jeter Street, Redwood City, CA 94062
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(54) Title: METHODS OF DIAGNOSIS OF CANCER COMPOSITIONS AND METHODS OF SCREENING FOR MODULATORS OF CANCER

(57) Abstract: Described herein are genes whose expression are up-regulated or down-regulated in specific cancers. Related methods and compositions that can be used for diagnosis and treatment of those cancers are disclosed. Also described herein are methods that can be used to identify modulators of selected cancers.



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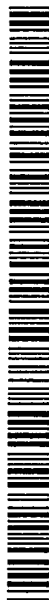
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- (71) Applicant (*for all designated States except US*): **EOS BIOTECHNOLOGY, INC.** [US/US]; 225A Gateway, Boulevard, South San Francisco, CA 94080 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): **AFAR, Daniel** [CA/US]; 435 Visitation Avenue, Brisbane, CA 94005 (US). **AZIZ, Natasha** [US/US]; 411 California Avenue, Palo Alto, CA 94306 (US). **GISH, Kurt, C.** [US/US]; 37 Artuna Avenue, Piedmont, CA 94611 (US). **HEVEZI, Peter, A.** [GB/US]; 1360 11th Avenue, San Francisco, CA 94122 (US). **MACK, David, H.** [US/US]; 2076 Monterey Avenue, Menlo Park, CA 94025 (US). **WILSON, Keith, E.** [US/US]; 219 Jeter Street, Redwood City, CA 94062 (US). **ZLOTNIK, Albert** [US/US]; 507 Alger Drive, Palo Alto, CA 94306 (US).
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/29560

A. CLASSIFICATION OF SUBJECT MATTER												
IPC(7) : C12Q 1/68												
US CL : 435/6												
According to International Patent Classification (IPC) or to both national classification and IPC												
B. FIELDS SEARCHED												
Minimum documentation searched (classification system followed by classification symbols) U.S. : 435/6, 7.1, 287.2; 436/63, 64												
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched												
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet												
C. DOCUMENTS CONSIDERED TO BE RELEVANT												
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.										
X,P --- Y,P	US 6,426,186 B1 (JONES et al.) 30 July 2002 (30.07.2002), see especially Detailed Description of the Invention and Sequence 62.	1-6 ----- 7										
X --- Y	US 6,194,158 B1 (KROES et al.) 27 February 2001 (27.02.2001), see especially Background of the Invention and Detailed Description of the Invention.	2-5 ----- 1, 6, 7										
X,P --- Y,P	US 6,440,676 B1 (KROES et al.) 27 August 2002 (27.08.2002), see especially Background of the Invention and Detailed Description of the Invention.	2-5 ----- 1, 6, 7										
Y,P Y	US 6,500,938 B1 (AU-YOUNG et al.) 31 December 2002 (31.12.2002), see especially Summary of the Invention and Description of the Invention. SMYTH TEMPLETON et al. Cloning and Characterization of Human Tumor Cell Interstitial Collagenase. September 1990, Volume 50, Number 17, pages 5431-5437, especially Figure 2.	1-7 1-7										
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.												
* Special categories of cited documents: <table border="0"> <tr> <td>*A* document defining the general state of the art which is not considered to be of particular relevance</td> <td>*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</td> </tr> <tr> <td>*B* earlier application or patent published on or after the international filing date</td> <td>*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</td> </tr> <tr> <td>*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</td> <td>*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</td> </tr> <tr> <td>*O* document referring to an oral disclosure, use, exhibition or other means</td> <td>*&* document member of the same patent family</td> </tr> <tr> <td>*P* document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>			*A* document defining the general state of the art which is not considered to be of particular relevance	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	*B* earlier application or patent published on or after the international filing date	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	*O* document referring to an oral disclosure, use, exhibition or other means	*&* document member of the same patent family	*P* document published prior to the international filing date but later than the priority date claimed	
A document defining the general state of the art which is not considered to be of particular relevance	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention											
B earlier application or patent published on or after the international filing date	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone											
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art											
O document referring to an oral disclosure, use, exhibition or other means	*&* document member of the same patent family											
P document published prior to the international filing date but later than the priority date claimed												
Date of the actual completion of the international search 03 March 2003 (03.03.2003)		Date of mailing of the international search report 24 MAR 2003										
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230		Authorized officer <i>Carolyn Smith</i> Carolyn Smith Telephone No. 703-308-0196										

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/29560

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet x

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-7 for Specie A(hemangiomas) and B (SEQ ID NO: 1)

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

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This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional examination fees must be paid.

Groups 1-104,648, claim(s) 1-7, drawn to a method for determining the presence or absence of a pathological (Specie A) cell in a patient via detection of polynucleotides that are at least 80% identical to listed sequences (Specie B). If electing from this Group Set, Applicants are asked to elect one species from A and B. Species A has 254 possibilities (see Table 1). Please note that the sequences in Tables 2A-68 are unsearchable as they are not included in the Sequence Listing. Applicants have supplied 412 nucleic acid sequences from which a selection can be made for Specie B. The total number of individual inventions in this Group Set including all possible combinations of Species A and B is 104,648.

Groups 104,649-105,060, claim(s) 8-12, drawn to an isolated nucleic acid molecules from Tables 2A-68, expression vectors, host cells, and polypeptides encoded by nucleic acid molecules with listed sequences from Tables 2A-68 (Species B). If electing from this Group Set, Applicants are asked to elect one species from Species B. Please note that the sequences in Tables 2A-68 are unsearchable as they are not included in the Sequence Listing. Applicants have supplied 412 nucleic acid sequences from which a selection can be made for Specie B. The total number of individual inventions possible in this Group Set with Specie B is 412.

Groups 105,061-105,472, claim(s) 13-14, drawn to an antibody that binds to a polypeptide encoded by a polynucleotide with sequences from Tables 2A-68 (Species B). If electing from this Group Set, Applicants are asked to elect one species from Species B. Please note that the sequences in Tables 2A-68 are unsearchable as they are not included in the Sequence Listing. Applicants have supplied 412 nucleic acid sequences from which a selection can be made for Specie B. The total number of individual inventions possible in this Group Set with Specie B is 412.

Groups 105,473-105,884, claim(s) 15, drawn to a method for targeting a compound to a pathological cell in a patient via administering an antibody that binds to a polypeptide encoded by a polynucleotide from Tables 2A-68 (Species B). If electing from this Group Set, Applicants are asked to elect one species from Species B. Please note that the sequences in Tables 2A-68 are unsearchable as they are not included in the Sequence Listing. Applicants have supplied 412 nucleic acid sequences from which a selection can be made for Specie B. The total number of individual inventions possible in this Group Set with Specie B is 412.

Groups 105,885-106,296, claim(s) 16-17, drawn to a method for determining the presence or absence of a pathological cell in a patient via contacting the sample with an antibody that binds to a polypeptide encoded by a polynucleotide from Tables 2A-68 (Species B). If electing from this Group Set, Applicants are asked to elect one species from Species B. Please note that the sequences in Tables 2A-68 are unsearchable as they are not included in the Sequence Listing. Applicants have supplied 412 nucleic acid sequences from which a selection can be made for Specie B. The total number of individual inventions possible in this Group Set with Specie B is 412.

Groups 106,297-106,708, claim(s) 18, drawn to a method for identifying a compound that modulates a pathology-associated polypeptide encoded by a polynucleotide that hybridizes to a sequence in Tables 2A-68 (Species B). If electing from this Group Set, Applicants are asked to elect one species from Species B. Please note that the sequences in Tables 2A-68 are unsearchable as they are not included in the Sequence Listing. Applicants have supplied 412 nucleic acid sequences from which a selection can be made for Specie B. The total number of individual inventions possible in this Group Set with Specie B is 412.

Groups 106,709-211,356, claim(s) 19, drawn to drug screening assay by administering a compound to a mammal or cell having a pathology (of Table 1) and comparing the level of gene expression of a polynucleotide that hybridizes to a sequence that is 80% identical to sequences as described in Tables 2A-68 (Species B) to gene expression in control cells or mammals. If electing from this Group Set, Applicants are asked to elect one species from A and B. Species A has 254 possibilities (see Table 1). Please note that the sequences in Tables 2A-68 are unsearchable as they are not included in the Sequence Listing. Applicants have supplied 412 nucleic acid sequences from which a selection can be made for Specie B. The total number of individual inventions in this Group Set including all possible combinations of Species A and B is 104,648.

This International Searching Authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2, and 13.3) for the reasons indicated below:

The inventions listed as all Group Sets (Groups 1-211,356) do not relate to a single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2 they lack the same or corresponding special technical features for the following reasons:

Groups 1-104,648 and Groups 105,472-211,356 are directed to methods or assays which vary in one or more of the following: reactants, steps, and/or goals which are not coextensive and which do not share the same technical feature. Groups 104,649-105,472 have two separate special technical features, a nucleic acid and an antibody, respectively. These are directed to different chemical entity types regarding the critical limitations featuring different structures and functions. The antibodies undergo recognition and binding reactions

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wherein what is bound is different from what is bound by the compositions including the nucleic acids. Thus, in summary, each Group is directed to a different special technical feature and thus supports this lack of unity.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

The claims in the Groups 1-104,648 and 106,709-211,356 include a series of species A directed to different pathologies which are listed in Table 1. Each of these types of pathologies are separate entities which affect patients differently, meaning each has its own special technical feature.

The claims in all Groups (1-211,356) include a series of species B directed to nucleic acid sequence listed (412 possibilities) which are considered separate as each defines its own special technical feature.

The first listed pathology (Specie A) and SEQ ID NO: 1 (Species B) will be automatically searched. For each additional Group with a specie combination elected, the fee is an additional \$210.00.

Continuation of B. FIELDS SEARCHED Item 3:

WEST, PUBMED, BIOSIS, CAPLUS, MEDLINE, SCISEARCH, EMBASE searching terms: diagnosis, cancer, screen, modulator, pathological cell, patient, nucleic acid, tissue, mRNA, detect, probe, blochip, array, therapeutic